IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Houghton et al. Application No.: 09/996,128 Filed: 11/27/2001 Title: Compositions for Treatment of Melanoma and Method of Using Same Attorney Docket No.: MSK.P-026-3 Customer No.: 52334	Group Art Unit: 1642 Examiner: A Harris Confirmation No: 3698

Commissioner for Patents

PO Box 1450

Alexandria, VA 22313-1450

RESPONSE TO FINAL REJECTION

Dear Sir:

This is in response to the Office Action mailed December 27, 2006 for the above-captioned application. Reconsideration and further examination are respectfully requested.

The examiner refused to withdraw the restriction requirement and consider Seq. ID No. 2. The Examiner has also failed to present any showing that "the sequences present unusual complications." as required. Thus, Applicants are filing a petition for review of the restriction requirement, and have not canceled the non-elected claims.

Claims 20-23, 29 and 30 stand rejected under 35 USC § 103 as unpatentable over the combination of Zhai et al in view of US Patent No. 5,773,291 and US Patent No. 6,080,727. Applicants again traverse this rejection.

The Examiner states that the Zhai reference teaches "a method of inducing specific T cell immunity for mammalian **metastatic** melanoma ... The administration was successful rendering a protective affect against murine **metastatic** melanoma. ... [T]he successful **metastatic** melanoma treatment presented in the entire article from 1996 establishes this treatment is well known" (Office Action, Page 4). In each of these instances, the Examiner refers to the melanoma of Zhai et al. as a metastatic melanoma, yet it is not so-described anywhere in the Zhai reference.

Therefore, if the examiner desires to maintain this assertion of fact, it must be supported by evidence that the cell line of Zhai et al was in fact a metastatic melanoma. *In re Ahlert*, 165 USPQ 418, 420-21 (CCPA 1970).

In fact, as reflected in the enclosed declaration of Alan Houghton, 1. B16 melanoma is not per se metastatic, and the parental B16 melanoma cells rarely metastasize. (Declaration, ¶ 3) The Zhai et al paper reports only B16 melanoma, and do not describe a metastatic derivative. Further, the tests performed in Zhai et al. have nothing to do with assessment of metastasis. (Declaration, ¶ 4). Finally, because B16 melanoma likely arose from a different source than the mucosal origin of CMM, and because B16 responds to drugs that are inactive against cutaneous and mucosal melanomas, it is not apparent that results for B16 provides any expectation of success in the treatment of CMM. (Declaration, ¶ 5).

The Examiner further states on Page 5 of the Office Action that "Applicants fail to take into account Zhai teaches the treatment of patients with metastatic melanoma, not just melanoma in a broad sense." As shown above, the Examiner's characterization of the Zhai paper as relating to a metastatic melanoma is in error. Furthermore, Zhai does not teach the treatment of patients in anything but the hypothetical. At Page 709, Col. 1, just before the Acknowledgments, Zhai states that "adenovirus-based tumor vaccines thus appear to be good candidates for use in clinical immunotherapy, although their ultimate benefits in clinical settings remain to be determined." This is nothing more than an invitation to experiment.

The '291 patent is cited for a teaching of expression of human tyrosinase and gp75. The Examiner argues that there is motivation to use these vectors in the method of Zhai et al. because "it is well known in the art that tyrosinase and gp75, quite like gp100, is recognized as a TAA implicated in the development of cancer vaccines and the Zhai treatment is advantageous." The Examiner has not responded on the merits to the Applicants argument that

> the references of record simply do not support this statement. Reference is made by the Examiner to a single sentence in Zhai et al,. which indicates that the identification of genes encoding TAA "has opened new possibilities for the development of cancer vaccines." There is a marked lack of congruence between this speculation concerning opportunities and the examiner's statement of what is "well-known" and what is reasonably likely to successful.

Instead, the Examiner has criticized Applicants saying they have not ":pointedly expressed wherein in Zhai this is found." (Office Action, Page 4) The statement in Zhai was one cited by the Examiner herself (Office Action of July 18, 2006, Page 5) but Applicants note for the record that it appears at Page 700, Col., 1 2nd paragraph.

In view of the foregoing, Applicants submit that maintaining the rejection of the claims under 35 USC § 103 is in error.

Furthermore, as previously noted, Zhai only discloses use of adenoviral vectors. Cancer antigens expressed in adenovirus and vaccinia virus are special cases. Even the self gene expressed in adenovirus and vaccinia gives immunity to cancer. For instance, Perricone et al. (Molecular Therapy 1:275-284, 2000) show that adenovirus vectors expressing either human and mouse gp100 inhibit tumor growth in mice. In addition, Overwijk et al. (PNAS 96:2092-2097, 1999) showed that vaccinia vector expressing mouse TRP-1 (also called TYRP1, gp75) inhibited mouse melanoma. Thus, in both cases the virus encoding the self gene inhibited growth of a mouse tumor. For plasmid DNA vaccines, DNA vaccination with the self-antigen does not result in tumor rejection. One needs the xenogeneic non-self DNA. The Zhai et al. paper shows xenogeneic gp100 works when delivered by the adenovirus, but this is a special type of vaccine (with substantial risks for use clinically) that also works for self-antigen. Thus, the Zhai et al. paper would not have predicted that xenogeneic plasmid DNA vaccine would work when self DNA vaccine did not.

Claim 30 specifies that the DNA immunization occurs in a non-viral plasmid vector. Notwithstanding the previous argument on this point, the Examiner has not explained why this claim is obvious over the cited combination of references.

Respectfully submitted,

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Enclosure

Rule 132 Declaration of Alan N Houghton